

Amendments to the Specification:

On page 1, please amend the paragraph spanning lines 11-23 as follows:

Biochips, also called biosensor chips, biological microchips, gene-chips or DNA chips, ~~consist~~include in their simplest form ~~[[of]]~~ a substrate on which a large number of different probe molecules are attached, on well defined regions on the chip, to which molecules or molecule fragments that are to be analyzed can bind if they are perfectly matched. For example, a fragment of a DNA molecule binds to one unique complementary DNA (c-DNA) molecular fragment. The occurrence of a binding reaction can be detected, e.g. by using fluorescent markers that are coupled to the molecules to be analyzed. This provides the ability to analyze small amounts of a large number of different molecules or molecular fragments in parallel, in a short time. One biochip can hold assays for 10-1000 or more different molecular fragments. It is expected that the usefulness of information that can become available from the use of biochips will increase rapidly during the coming decade, as a result of projects such as the Human Genome Project, and follow-up studies on the functions of genes and proteins.

On page 2, please amend the paragraph spanning lines 14-17 as follows:

It is a problem that the magneto-resistive sensor element does not allow a sensitive detection in the mV or even μ V range ~~which is necessary~~ to detect for instance a single magnetic particle functioning as a label for molecular diagnostics biological sample analysis, or chemical sample analysis.

On page 2, please amend the paragraph spanning lines 23-25 as follows:

~~The object according to the invention is achieved in that cross-talk~~
Cross-talk suppression means are present for suppressing cross-talk between the magnetic sensor element and the at least one magnetic field generator.

On page 2, please amend the paragraph spanning lines 26-31 as follows:

~~The invention is based on the insight that cross-talk~~ Cross-talk is a limitation for the sensitivity of detection of small magnetic fields. The cross-talk can be subdivided in capacitive cross-talk and magnetic cross-talk. Reduction of the capacitive and/or the magnetic cross-talk is important, in particular when the measurement frequency increases. The on-going down-scaling of the dimensions on chips increases both the capacitive as well as the magnetic cross-talk.

On page 3, please amend the paragraph spanning lines 8-12 as follows:

The cross-talk suppression means can comprise ~~[[and]]~~ an electrostatic shielding device between the magnetic sensor element and the magnetic field generator. The electrostatic shield may be any device, which attenuates coupling between the conductor and the sensor. This electrostatic shield can be implemented by a conductive layer between conductor and sensor, which conductive layer is connected to a fixed voltage such as ground.

On page 4, please amend the paragraph spanning lines 32-35 as follows:

~~The method according to the invention is achieved in that cross-talk~~
suppression means are used to reduce cross-talk between a magnetic sensor element and at least one magnetic field generator for generating a magnetic field.

On page 8, please amend the paragraph spanning lines 17-27 as follows:

A biosensor device 50 is represented schematically in Fig. 5A. It comprises a cartridge housing 51, chambers 52 and/or channels 53 for containing the material, e.g. analyte to be analyzed, and a biochip 54. The biochip 54 is a collection of miniaturized test sites (micro-arrays) arranged on a solid substrate that permits many tests to be performed at the same time in order to achieve higher throughput and speed. It can be divided into tens to thousands of tiny chambers each containing bioactive molecules, e.g. -short DNA strands or probes. It can be three dimensional, capable of running as many as 10,000 different assays at the same time. Or, the chip 54 can be manufactured more simply with as few as 10 different assays running at one time. In addition to genetic applications (decoding genes), the biochip 54 is being used in toxicological, protein, and biochemical research, in clinical diagnostics and scientific research to improve disease detection, diagnosis and ultimately prevention.

On page 9, please amend the paragraph spanning lines 19-29 as follows:

In Fig. ~~[[1B]]~~ 5B, sensor molecules 58 labeled with magnetic particles 15 are able to selectively bind target sample 57. When random searches are performed, e.g. screening in which DNA binding proteins of a certain tissue extract bind to a grid with a library of nucleotides, the sensor molecule should have a very broad specificity. In this example a sensor molecule with a spacer reactive towards amino groups or carboxy groups would be useful. Other sensor molecules with a reactive group towards sugars, DNA are also suitable. In the case of a direct search, tailor-made sensor molecules can be used e.g. where a screening with a protein against a protein library is performed for assumed protein-protein interaction, an antibody is an obvious choice. Both monoclonal and polyclonal antibodies may be used. As shown in Fig. ~~[[1B]]~~ 5B, magnetic particles 15 are indirectly bound to the target sample 57.

On page 10, please amend the paragraph spanning lines 3-8 as follows:

The functioning of the biochip 54 is as follows. Each probe element 55 is provided with binding sites 56 of a certain type. Target sample 57 is presented to or passed over the probe element 55, and if the binding sites 56 and the target sample 57 match, they bind to each other. Magnetic particles 15 are directly or indirectly coupled to the target sample 57, as illustrated in Figs. ~~[[1B]]~~ 5B, ~~[[1C]]~~ 5C and ~~[[1D]]~~ 5D. The magnetic particles 15 allow to read out the information gathered by the biochip 54.

On page 10, please amend the paragraph spanning lines 15-26 as follows:

In a first embodiment the device according to the present invention is a biosensor and will be described with respect to Fig. 6 and Fig. 7. The biosensor detects magnetic particles in a sample such as a fluid, a liquid, a gas, a visco-elastic medium, a gel or a tissue sample. The magnetic particles can have small dimensions. With nano-particles are meant particles having at least one dimension ranging between 0.1 nm and 1000 nm, preferably between 3 nm and 500 nm, more preferred between 10 nm and 300 nm. The magnetic particles can acquire a magnetic moment due to an applied magnetic field (e.g. they can be paramagnetic) or they can have a permanent magnetic moment. The magnetic particles can be a composite, e.g. ~~consist of~~ include one or more small magnetic particles inside or attached to a non-magnetic material. As long as the particles generate a non-zero response to the frequency of an ac magnetic field, i.e. when they generate a magnetic susceptibility or permeability, they can be used.

On page 10, please amend the paragraph starting on line 27 and continuing to page 11, line 9 as follows:

The device may comprise a substrate 10 and a circuit e.g. an integrated circuit. A measurement surface of the device is represented by the dotted line in Fig. 6 and Fig. 7. In embodiments of the present invention, the term “substrate” may include any underlying material or materials that may be used, or upon which a device, a circuit or an epitaxial layer may be formed. In other alternative embodiments, this “substrate” may include a semiconductor substrate such as e.g. a doped silicon, a gallium arsenide (GaAs), a gallium arsenide phosphide (GaAsP), an indium phosphide (InP), a germanium (Ge), or a silicon germanium (SiGe) substrate. The “substrate” may include for example, an insulating layer such as a SiO₂ or an Si₃N₄ layer in addition to a semiconductor substrate portion. Thus, the term substrate also includes glass, plastic, ceramic, silicon-on-glass, silicon-on sapphire substrates. The term “substrate” is thus used to define generally the elements for layers that underlie a layer or portions of interest. Also, the “substrate” may be any other base on which a layer is formed, for example a glass or metal layer. In the following reference will be made to silicon processing as silicon semiconductors are commonly used, but the skilled person will appreciate that the present invention may be implemented based on other semiconductor material ~~device-s~~ devices and that the skilled person can select suitable materials as equivalents of the dielectric and conductive materials described below.

On page 20, please amend the paragraph spanning lines 9-17 as follows:

The magnetic particle concentration is determined as a function of the x-position by a frequency multiplex method, which is illustrated in Fig. 21. An anti-phase current in conductor ~~[[12B]]~~ 12b compensates the cross-talk signal originating from conductor 12a at frequency f₁ shown in Fig. 20. Likewise an anti-phase current in conductor 12a compensates the crosstalk from conductor 12b. An additional effect

of this embodiment is that the net field distribution sensor device changes towards an odd function. Figure 20 shows the field characteristic at frequency f_1 .

On page 20, please amend the paragraph spanning lines 18-29 as follows:

In Fig. 21 a first modulating signal $\text{Mod}_1(t)$ is sent from a first source 20a to the first conductor 12a to modulate the current I_1 and is sent to a first demodulating multiplier 22a. The modulated current I_1 which flows through the conductor 12a induces a magnetic field, shown by field lines 14 in Fig. 19, which is mainly oriented perpendicular to the plane of the sensor element 11 at the location of the sensor 11. When magnetic particles 15 are present in the neighborhood of the sensor 11, the magnetic field at the location of the sensor 11 and thus the resistance of the sensor 11 is changed. The change of resistance gives rise to a different voltage drop over the sensor 11 and hence a different measurement signal delivered by the sensor 11. The measurement signal is sent through an amplifier 21 and the amplified measurement signal $\text{Ampl}(t)$ is demodulated with the first modulating signal $\text{Mod}_1(t)$. The resulting first intermediate signal $\text{Mult}_1(t)$ is then sent through a first low pass filter [[23A]] 23a to form a first detection signal $\text{Det}_1(t)$.

On page 20, please amend the paragraph spanning lines 30-34 as follows:

The current I_2 in the second conductor 12b is modulated by a second modulating signal $\text{Mod}_2(t)$. The second modulating signal is sent to a second demodulating multiplier [[22B]] 22b where it is demodulated with the amplified measurement signal $\text{Ampl}(t)$, thus forming a second intermediate signal $\text{Mult}_2(t)$. The second intermediate signal $\text{Mult}_2(t)$ is then sent through a second low pass filter 23b to form a second detection signal $\text{Det}_2(t)$.

On page 21, please amend the paragraph starting on line 30 and continuing to page 22, line 5 as follows:

Fig. 22 shows a seventh embodiment for reducing the capacitive cross-talk without affecting the magnetic field. For didactic reasons one half of the detection schema is depicted, namely only that part that measures at frequency f_1 . An anti-phase voltage in conductor 12b compensates the capacitive crosstalk signal originating from the current in Conductor 12a at frequency f_1 . For this purpose the ground connection of Conductor 12b is removed so that no current can flow to ground. Measuring at f_2 is performed in an analogous way by disconnecting the ground connection from Conductor ~~[[12A]]~~ 12a and feeding an anti-phase voltage to Conductor 12a.